BRITISH MEDICAL BULLETIN

Vol. 1. (1943) No. 7

The object of this Bulletin is to provide a guide to medical science and thought in Britain, and it consists mainly of summaries of a representative selection of British papers on subjects of medical interest. Any material appearing in the Bulletin may be published without fee, but acknowledgment of the source, by addition of the initial letters BMB followed by the serial numbers of the items selected, would be appreciated.

PERIPHERAL NERVES

SPECIAL CONTRIBUTION

RECENT WORK ON PERIPHERAL NERVE INJURIES
by Professor H. J. Seddon ... 74

DIAGNOSIS AND THERAPEUTICAL PROCEDURES

A New Classification of Nerve Injuries ... 76
Nerve Block in the Investigation of Peripheral Nerve Injuries ... 76
Innervation and Function of the Thenar Muscles ... 76
Splintage of Peripheral Nerve Injuries ... 76
Fibrin Suture of Peripheral Nerves in Animals ... 77
Fibrin Suture of Human Nerves ... 77
Various Materials in Experimental Nerve Suture ... 77
Amnioplastin in Peripheral Nerve Injuries ... 77
Repair of Large Gaps in Peripheral Nerves ... 77
Degeneration and Re-Innervation of Nerve Grafts ... 78
Histological Condition of a Nerve Autograft in Man ... 79
Functional Recovery after Nerve Grafts ... 79
Chemical Inhibition of Fibre Regeneration and Neuroma Formation ... 80
Local Application of Sulphanilamide to Peripheral Nerves ... 80

TRACTION INJURIES OF NERVES

Traction Injuries to Nerves in the Human Subject ... 80
Experimental Traction Nerve Injuries in Animals ... 80

FACTORS AFFECTING NERVE RECOVERY AND REPAIR

Recovery of Motor Function after Nerve Lesions ... 81
Recovery of Sensory Function after Nerve Lesions ... 81

THE ACTUAL PROCESSES OF NERVE REPAIR

Regeneration after Immediate and Delayed Suture ... 82
The Outwandering of Cells from Degenerating Nerves ... 82
Recovery of Fibre Numbers and Diameters ... 83
Rate of Regeneration ... 83
Early Degeneration of Cutaneous Fibres ... 83
Local Extension of Cutaneous Nerve Fibres ... 84
Axonal Regeneration in Cutaneous Nerve Plexuses ... 84
Structure of Connective Tissue Sheaths of Cutaneous Nerves ... 84

THE BLOOD VESSELS OF PERIPHERAL NERVES

Historical Review ... 84
Effects of Ligation of Regional Vessels ... 84

REGENERATION IN THE CENTRAL NERVOUS SYSTEM

Influence of Spinal Ganglia and Nerve Fragments Grafted into the Brain ... 85
Insertion of Peripheral Nerve Stumps into the Brain ... 85

OBSERVATIONS ON DENERVATED MUSCLE

Effect of Electrotherapy ... 85
Clinical Application of Electromyography ... 86

Bibliography of Other Relevant Papers ... 86

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SPECIAL CONTRIBUTION

RECENT WORK ON PERIPHERAL NERVE INJURIES

by PROFESSOR H. J. SEDDON, D.M., F.R.C.S.

Although the peripheral nervous system has excited the constant interest of many experimental workers and a few neurologists, the clinical problems presented by nerve injuries have not received great attention except during times of war. This is due to the fact that the injuries of warfare involve peripheral nerves with a frequency far greater than that found in the injuries of civil life. Yet in this age of increasing mechanisation, with its toll of accidents which resemble more and more the injuries of warfare, the frequency, and, therefore, the importance of nerve injuries in civil practice, will almost certainly increase. Thus, there is much to be said for maintaining in peace-time the interest and perhaps, in some measure, the clinical organisations that have been engendered by the war. Indeed, the volume of routine work that has to be done in war-time is, to some extent, a hindrance to the pursuit of clinical research in a field where the work is notoriously time-consuming. The answers to many of the questions that now confront us can hardly be sought until those interested are freed from the mass of curative work that now occupies most of their time.

Early in 1940, the British Ministry of Health and the *Medical Research Council* (and later the Department of Health in Scotland), profiting from lessons learned during the last war, set about organising five Centres for the treatment of peripheral nerve injuries, three in England, and two in Scotland. The centres have been established at civilian hospitals in the *Emergency Medical Service* (Ministry of Health), and at each of these, certain members of the staff have made it their business to devote much of their time to the investigation and treatment of nerve injuries and, as the work has increased, to building up clinical teams. By arrangement between the Ministry of Health and the Fighting Services, all Army and R.A.F. cases of nerve injury are directed to one or other of the centres. Civilians eligible for admission to an *Emergency Medical Service* hospital are also provided for, and the result is that a high degree of segregation has been achieved.

The expenses incidental to this work come under four headings:

(i) *Cost of Maintenance of the Patient in Hospital.* This is borne by the Ministry of Health in precisely the same way as applies in the case of other Service casualties, pensioners, and civilian war casualties.

(ii) *Payment of Staff.* At certain centres some or all of the workers are full-time salaried officers in the *Emergency Medical Service.* In some cases, the *Medical Research Council* has provided the salaries of research workers and grants for expenses.

(iii) *Secretarial Staff.* The clerical work is exceedingly heavy, and receives the financial support of the Ministry of Health. The notes are often lengthy and have to be kept in triplicate, so that copies are available for the interested Government departments. In addition, there is a great volume of correspondence with the Ministry of Pensions, and with local hospitals where patients receive treatment after leaving hospital.

(iv) *Patients' Expenses.* Perhaps the most noteworthy feature of the organisation is the provision made for regular follow-up examination. So that patients may suffer no hardship, free travelling warrants are provided whenever their attendance for re-examination is requested; and in certain circumstances compensation is made for loss of wages during the day or two when the man is away from work. As a measure of economy the patient attends the centre nearest to his home, and if this happens to be a centre other than the one at which he was first treated, a copy of the notes is sent to the surgeon who becomes responsible for the follow-up examinations. The only flaw in the scheme is the absence of any provision in cases where the injury is not attributable to the war. A man in the fighting services who is the victim of an ordinary accident while on leave is at present eligible neither for a pension nor for the benefits that make regular follow-up examination feasible.

Until recently there was no provision in the Fighting Services for the systematic treatment of nerve injuries; indeed, it was considered undesirable, since most of the patients would require treatment over a long period, and many would inevitably be discharged as unfit for further service. However, the accumulation in South Africa of numbers of casualties from the Middle East required a special remedy, and a Nerve Injuries Centre has recently been established at a military hospital in Natal; others have been organised in India and the Middle East.

This segregation of patients allows rehabilitation to be arranged in a way that is specially adapted to the disabilities which result from injuries to main nerve trunks. At Oxford, a convalescent centre with 70 beds has been established at a large house about five miles from the hospital.

Rehabilitation takes two forms: (*a*) *General*—physical training, games, orderly duties, lectures and entertainments—such activities as are required to keep men fit mentally and physically; and (*b*) *Specific*—remedial work designed to encourage fine co-ordinated movements of the hands and the improvement of tactile discrimination. This work includes weaving, basket making, toy making, clay modelling and carpentry. A patient recovering from paralysis of the ulnar nerve needs, above all, to develop good control of the intrinsic muscles of the fingers, while one recovering from median palsy must be taught to make the best possible use of such cutaneous sensibility as returns to the thumb, index and middle fingers.

It is often possible for a man to return to work, or even to military service, long before recovery is complete. Over-stretching of paralysed muscles can be prevented by the application of splints designed to protect muscles without limiting movement. In the Fighting Services, this early return to work is made possible chiefly by the increasing specialisation in methods of warfare, and by the readiness of the Services to find work suited to a man's inclinations and physical capacity. As soon as an R.A.F. pilot with external popliteal paralysis has regained full passive movement in the joints of his foot, and has been fitted with a toe-raising spring, he may return to flying—sometimes operational flying—without waiting for recovery in the anterior tibial and peroneal muscles. The same is true of patients with ulnar paralysis. These men continue with their treatment while on active service, care being taken to post them to a station near to a hospital where treatment is available.

Ultimately, some patients make such excellent recovery (mostly radial nerve injuries) that they can be placed in a high category: an enthusiastic young corporal, who had had a tendon transplantation performed because of irreparable damage to the radial nerve, recently wrote from North Africa: "My job during the whole advance was driving a five-ton armoured car, in which I had plenty of exciting moments. I have avenged the wound I received at Dunkirk."

However, such complete restoration of function occurs in only a minority of cases, and many men must leave the Services and return to civil life. It is remarkable how many are able to go back to their old employment; if training in a new occupation is required, the Ministry of Labour takes care of them, and the Government training schemes, started two years ago, are now working well.

In the war of 1914–18, the organised treatment of nerve injuries was due to the efforts of Major-General Sir Robert Jones, Inspector of Military Orthopædics. At his instigation, cases were segregated at a number of centres, and several of them were placed under the care of orthopædic surgeons. It seemed to him that as nerve injuries were frequently associated with injuries to bones, joints, tendons and muscles, the work could best be done by men specially interested in the surgery of the limbs, that is, orthopædic surgeons. This arrangement, peculiar to the United Kingdom, has to some extent been followed in the present war, and at three of the centres the Directors are orthopædic surgeons. There are undoubted merits in the plan, but the responsible surgeon must either take the trouble to become a neurologist himself, so far as the peripheral nervous system is concerned, or he must work in close collaboration with a neurologist. However, the interest and ability of the man are of far greater importance than his professional designation, and the arrangement made at any one centre depends primarily on the local talent available. There is much to be said for the surgeon who is prepared to immerse himself in the minutiæ of neurological diagnosis, for his approach to a case will then be more enlightened than that of the surgeon who is little more than a technician, exploring a nerve under the direction of the neurologist.

Research may be considered under three headings:

(i) *Documentation and Analysis of Clinical Material.* This not only provides a necessary check on the efficacy of various forms of treatment but may lead to the clearer definition of various types of nerve injuries. A preliminary note (Seddon, 1942) has already been published on a classification of nerve injuries which covers the majority of lesions encountered in clinical practice. This classification is now being worked out in greater detail especially in regard to partial lesions. Elkington (1942) has published a short account of nerve injuries produced by the injection of drugs of the sulphonamide group. Other work is now in progress on the classification of nerve injuries due to traction, to ischæmia, and to compression of nerves by sub-fascial effusions (Parkes, unpublished work at the Glasgow Centre).

(ii) *Special Methods of Examination.* It is often possible, by the employment of such methods, to obtain from patients information of a kind that would be difficult or impossible to elicit by other means. Highet (1943) has shown that in three cases out of four, one or more of the thenar muscles are innervated by the ulnar nerve. By blocking nerve trunks with a local anæsthetic (1942) he has shown how anomalous cutaneous or motor innervation may be elucidated; by employing a simplified electromyograph, Weddell, Feinstein & Pattle (1943) have provided an easy means for determining whether a muscle is normally innervated, partially innervated, denervated, or completely destroyed; and Richards at Edinburgh [unpublished work] is using skin temperature measurements as an index of vasomotor disturbances resulting from nerve injury.

(iii) *Animal Experiment.* Lastly, animal experiment may be employed to determine the precise nature of the changes in nerve and muscle consequent on various kinds of nerve injury.

It is only by a balanced combination of clinical observation and animal experiment, however, that steady progress can be made. On the one hand, animal experiment permits the observer to examine his material in elaborate detail; on the other, certain observations can be made only on subjects who can describe their experiences with some accuracy—the investigation of cutaneous sensibility has been almost entirely dependent on the services of the human volunteer. Hence, it is important that laboratory and clinical investigators should work together or, at least, examine each other's work fairly frequently. Laboratory experiment may explain the shortcomings of a generally accepted operative procedure—for example, the work of Highet, Holmes & Sanders (1943) on the deleterious effect of post-operative stretching on nerves, after extensive resection and suture. By contrast, a laboratory technique, ideal in animal experiments, may prove of only limited value in clinical practice; for example, fibrin suture of nerves (Seddon & Medawar, 1942). Precise methods for working out the rates of regeneration of nerves were elaborated experimentally in animals (Gutmann, Guttmann, Medawar & Young, 1942); these, in turn, led to the development of a method for working out rates of regeneration in man (Seddon, Medawar & Smith, 1943), which revealed something that had not been shown in the animal experiments, namely, that the rates of regeneration are not uniform—they fall off as the process approaches completion.

This local co-ordination of the work of the clinician and the experimental biologist has been expanded to cover the work at all five centres.

The Peripheral Nerve Injuries Committee of the *Medical Research Council* meets regularly under the chairmanship of Brigadier George Riddoch, a pupil of Henry Head; he is Consulting Neurologist to the Army, and Consultant Adviser on Nerve Injuries to the Ministry of Health. It is the business of this Committee, not only to stimulate research and to survey progress, but to see that there is no unnecessary duplication of effort. There is also a liaison with the Neurological and Neurosurgical Committees of the *National Research Council* of the United States, helped by a free interchange of bulletins describing the work being done at centres in both countries.

In this way, knowledge is slowly but surely being accumulated, and put to use in practice. The clinical records are kept in such a way that after the war a *corpus* of detailed information will be available for analysis. Between 3,000 and 4,000 patients have already been treated at the Centres; ultimately, this great and constantly increasing mass of material should provide a very complete picture of this fascinating field of neurology.

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[6] [*See BMB* **113**] [7] [*See BMB* **118**] [8] [*See BMB* **142**]

Professor H. J. Seddon has occupied the Chair of Orthopædic Surgery at Oxford since January, 1940. He is Clinical Director of the Wingfield-Morris Hospital and of the Nerve Injuries Centre that has been established there. Nearly 1,000 patients have passed through this Centre since July 1940, and most of them are still under observation.

The experimental work at Oxford is carried out, for the most part, in the Department of Zoology and Comparative Anatomy. All the workers, headed by Dr. J. Z. Young, are biologists. Yet they frequently work in the hospital, and the clinicians in the laboratory. The Centre as a whole provides a good example of the benefits that derive from the joining of forces of a purely scientific with those of a clinical department.

[*In the article on pages 74–75, the organisation and methods adopted in Britain for the segregation and study of peripheral nerve injuries are outlined. The rest of this issue is devoted to reviews of recent published work on this subject, most of which has been carried out at the Oxford Nerve Injuries Centre and in the University Scientific Departments at Oxford and Birmingham. Special acknowledgment is due to one of the Oxford workers, F. K. Sanders, for having contributed the majority of the abstracts published below.*]

DIAGNOSIS AND THERAPEUTICAL PROCEDURES

113

A CLASSIFICATION OF NERVE INJURIES

by H. J. Seddon, *British Medical Journal*, **2**, 237–239, 29/8/42

British neurologists normally recognize three fundamental types of nerve injury, namely nerve "contusion," "compression," and "concussion." However, while these terms hint at the cause of injury, they do not describe the actual effect of the injury on the nerve itself. In this paper the author, who is Nuffield Professor of Orthopædic Surgery at Oxford, proposes a classification of nerve injuries in terms which are descriptive of the lesions themselves. Nerve injuries are divided into three classes, namely:

(i) *Neurotmesis*, in which the nerve has been completely divided, and a complete sensory and motor paralysis develops, from which recovery cannot take place spontaneously.

(ii) *Axonotmesis*, in which the nerve fibres are damaged to such an extent that complete peripheral degeneration occurs, but the perineurium and the more intimate supporting structures of the nerve remain in continuity, and spontaneous recovery by regeneration can occur. The clinical signs, however, are still those of complete paralysis.

(iii) *Neurapraxia*, used to describe paralyses so short-lived that recovery from them cannot possibly be due to regeneration. Paralysis in this type is rarely complete, and its clinical characteristics are:

(*a*) the paralysis is predominantly motor;
(*b*) there is little muscle wasting or loss of electrical reactions;
(*c*) subjective sensory disturbances, such as tingling, numbness, burning, are common;
(*d*) objective evidence of disturbances of sensibility to touch, pain, cold, or warmth is rare;
(*e*) there is often a loss of postural or vibration sense;
(*f*) there is rarely any loss of sweating.

The classification is based on a study of 460 cases at the Oxford Peripheral Nerve Injury Centre. Obviously, all cases of peripheral nerve injury cannot be classified under these three simple headings. Injury frequently affects different parts of the nerve, or different fibres, to varying degrees, and the clinical picture is thus often complex. However, all cases can be effectively described by combinations of two or three of the types defined above.

114

PROCAINE NERVE BLOCK IN THE INVESTIGATION OF PERIPHERAL NERVE INJURIES

by W. B. Highet, *Journal of Neurology and Psychiatry*, **5**, 101–129, July & October 1942

This paper from the Nuffield Department of Orthopædic Surgery, Oxford, illustrates the value of peripheral nerve block as a diagnostic procedure in cases of peripheral nerve injury. The author describes a technique by means of which any nerve may be located and anæsthetised for a period of from one to three hours. This is done in the following way: A hypodermic syringe containing the solution (2% procaine with 0·002% adrenalin) used to anæsthetise the nerve, is attached to a fine needle, electrically insulated by means of a phenyl resin except for 1 or 2 mm. at its tip, and connected to one pole of a faradic coil. The other pole leads to a broad moist plate applied to some neutral area such as the back of the thigh. When the current is turned on and the needle inserted, its tip acts as a unipolar stimulating electrode, and as soon as the nerve is touched the patient experiences a tingling sensation over the peripheral distribution of the nerve. When the nerve has been found in this way, the anæsthetic is injected either intraneurally (2 cm.^{3}) or else around the nerve (5–10 cm.^{3}).

Nerve block by procaine is regarded as complete when the following conditions are observed: (*a*) vasodilation, anhidrosis, and analgesia throughout the autonomous zone of the skin area supplied by the nerve; (*b*) complete and lasting paralysis of muscles supplied by the nerve distal to the site of block.

This method has been found useful by the author as a means of investigating (i) anomalous innervation of muscles, (ii) supplementary and trick movements, (iii) sensory and sudomotor distribution of peripheral nerves, in relation to the differentiation of complete and incomplete or recovering lesions, (iv) the vasomotor distribution of peripheral nerves.

The usefulness of nerve block in these various connections is demonstrated by reference to 13 cases treated by the author.

115

INNERVATION AND FUNCTION OF THE THENAR MUSCLES

by W. B. Highet, *Lancet*, **1**, 227–230, 20/2/43

According to the classical description, the thenar muscles fall into two groups: (1) those lying superficial to the tendon of *flexor pollicis longus* and innervated by the median nerve, and (2) those lying deep to this tendon, which are innervated by the ulnar nerve. Many authors, however, have pointed out that considerable variations in the nerve supply of these muscles exist (*see* Foerster, 1929).

The present author has analysed 20 cases of median nerve paralysis at the Wingfield-Morris Orthopædic Hospital, Oxford, by direct stimulation of the nerves through the skin, and by means of the technique of procaine nerve block which he describes elsewhere (Highet, 1942). In 16 cases *flexor pollicis brevis* was active; in 4 cases there was action in *opponens pollicis* in addition; and in 2 cases *abductor pollicis brevis* also participated in the action. All of these muscles are normally innervated by the median nerve, so in 16 out of 20 cases the innervation of the thenar muscles was anomalous. In all of them the anomalous innervation came from the ulnar nerve.

The author points out that it is important to realise that anomalous innervation of these muscles frequently occurs, as faulty diagnosis of an incomplete or recovering lesion has been made in many cases of complete division of the median nerve because of good action in one or more of the thenar muscles. This has led to an unnecessary delay in the performance of nerve suture.

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116

SPLINTAGE OF PERIPHERAL NERVE INJURIES

by W. B. Highet, *Lancet*, **1**, 555–558, 9/5/42

In this paper from the Wingfield-Morris Orthopædic Hospital, the author describes the general principles of peripheral nerve injury splintage and the types of splint in use at the Oxford Peripheral Nerve Injury Centre.

The following are the principles which must be observed in correct splintage of nerve injuries:

(1) *Avoidance of stretching* of paralysed muscles either by gravity or the action of antagonists. The paralysed muscles must be splinted so that their points of origin are approximated to their points of insertion.

(2) *Avoidance of immobilisation.* All joints of the paralysed limb must be allowed as full a range of movement as is compatible with the relaxation of paralysed muscles. Continual immobilisation of joints leads to stiffness and permanent disability.

(3) *Avoidance of pressure.* The splint must not press on an analgesic area of skin or interfere with the circulation.

(4) *Occupational therapy.* Splints must be such that the

patient can return to work, or carry out occupational therapy, while still wearing them.

All splints must be removed for half an hour twice every day, when physiotherapy is carried out and each joint of the limb put through its full range of passive movement. Although this involves the transient stretching of paralysed muscles, the result is probably not harmful.

At the Oxford Centre the following types of splint are employed:

(i) For *median* palsy. An elastic splint is used to hold the thumb in a position of palmar adduction and opposition. This is necessary to prevent adduction contracture of the thumb.

(ii) For *ulnar* palsy. A 'knuckle-duster' splint is employed, which holds the fingers in slight flexion at the metacarpo-phalangeal joints, and prevents stretching of the *interossei* and *lumbricales*. The splint also prevents the development of a claw hand, since, when the fingers are in slight flexion, the *extensor communis digitorum* can extend the interphalangeal joints.

(iii) For *radial* palsy. An elastic extension splint is employed, similar to that recommended by the *Medical Research Council* after the last War. In this palsy the fingers must never be immobilised, and a fixed full-length splint which places the wrist joint in full extension should be avoided.

(iv) For *circumflex* and *brachial plexus* palsy. An abduction splint is used with a universal joint in the elbow part. This avoids the stiffness of the shoulder and elbow which follows the use of a fixed splint.

(v) For *sciatic* palsy. Side-irons, hinged at the ankle, and a toe-raising spring are used.

In conclusion the author states that splints should be applied as soon as possible after injury, but that improper splintage is worse than no splintage at all.

117

FIBRIN SUTURE OF PERIPHERAL NERVES

by J. Z. Young & P. B. Medawar, *Lancet*, **2**, 126–128, 3/8/40

Suture of peripheral nerves by stitches, even if these are restricted as far as possible to the epineurium, produces considerable disorganisation of the regenerating nerve fibres. In this paper from the Department of Zoology and Comparative Anatomy, Oxford, the authors describe how the cut stumps may be stuck together by means of a concentrated plasma gel. The stumps are held together, and concentrated plasma freshly mixed with a strong tissue extract is poured round them. In about ½–2 minutes the plasma clots to a firm jelly which adheres to the nerves and holds the stumps together. The gel remains long enough to allow a firm union to be established between the divided ends.

The concentrated plasma was prepared from cockerel blood. This is withdrawn from the carotid artery (about 100–150 cm.³ could be obtained from a single bird) through oiled cannulæ into large centrifuge tubes. These are packed in ice for 10 minutes and then centrifuged, after which the supernatant plasma can be easily separated. From part of this plasma the fibrinogen is precipitated. One volume of blood is mixed with 9 volumes of redistilled water, and then with 0·10–0·15 volumes of a 1% (by volume) solution of acetic acid in redistilled water. The flocculate of fibrinogen is centrifuged off, and can be redissolved in the appropriate volume of untreated plasma to make concentrated fibrinogen solutions of any strength up to ten times normal.

The method proved very effective for joining the cut ends of the sciatic nerve in the rabbit and the dog. Nerve fibres grew slightly faster across such a junction than across the scar of a stitched nerve, and good funicular apposition was secured.

118

FIBRIN SUTURE OF HUMAN NERVES

by H. J. Seddon & P. B. Medawar, *Lancet*, **2**, 87–88, 25/7/42

The authors report the use of the concentrated fibrinogen solution introduced by Young & Medawar (1940) in a number of nerve sutures at the Wingfield-Morris Orthopædic Hospital at Oxford. They conclude that the method is of value for the primary suture of divided nerves, but is less useful for secondary suture because of the tension which follows resection of a length of nerve. The material is especially useful for the placing of nerve grafts.

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119

EXPERIMENTAL STUDY OF NERVE SUTURE WITH VARIOUS MATERIALS

by L. Guttmann, *British Journal of Surgery*, **30**, 370–375, April 1943

In spite of wide experience during the last War, and the clear-cut experimental results of Sargent & Greenfield (1919), there is as yet no unanimity of opinion as to the most satisfactory suture material for nerves. The present author, working in the Department of Zoology and Comparative Anatomy at Oxford, made a number of nerve sutures in rabbits, using plain sterile catgut, plain white silk, green silk, waxed and unwaxed black silk, and woman's hair as suture materials. Whatever material was used it always produced undesirable cellular and fibrous reactions, which provided obstacles to the outgrowth of new axons. Woman's hair and plain white silk provoked the least reaction, and of these two, woman's hair, by virtue of its small calibre and smooth surface, allowed the neatest stitching and caused least damage to the nerve.

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120

EXPERIENCES IN THE TREATMENT OF PERIPHERAL NERVE INJURIES WITH AMNIOPLASTIN

by L. Rogers, *British Medical Journal*, **1**, 587, 19/4/41

The amnioplastin used was prepared in the Surgical Unit at Cardiff from placentas obtained from the Obstetrical Department. The method of preparation was that described by Chao, Humphreys & Penfield (1940), and Penfield (1940), and the membranes were preserved in 70% alcohol in stoppered bottles. Before use, the amnioplastin was boiled for half an hour in distilled water.

The membrane was used in 12 cases of injury involving peripheral nerves: ulnar 2, median 4, musculo-spiral 1, great sciatic 2, external popliteal 3. The author refers also to the use of amnioplastin in 8 intracranial cases.

Except in one intracranial case, all wounds healed by first intention. Early functional restoration was noted in most, and freedom from pain in all. The relief of pain, cessation of sweating, and early restoration of normal skin appearances in two cases of causalgia were particularly striking.

The author concludes that amnioplastin is a valuable material for the isolation of nerve elements.

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121

THE REPAIR OF LARGE GAPS IN THE PERIPHERAL NERVES

by F. K. Sanders, *Brain*, **65**, 281–337, September 1942

Resection of the damaged portion of nerve is a standard procedure in the repair of the peripheral nerve injuries of warfare, and as a result a considerable gap is often left between the stumps. Direct coaptation, with the limb in the normal position, is thus rarely possible. Methods have been devised for closing these gaps, and they may be classified as follows: *Bridge operations*, in which some sort of bridge is used to carry the new fibres across the gap between the stumps,

namely, nerve grafts, double lateral implantation, nerve flap operations, *suture à distance*, and tubulisation; *manipulative nerve operations*, in which every means is employed to achieve end-to-end apposition of the resected stumps by mobilisation, transposition, flexion of joints followed by nerve stretching, and bulb suture; *nerve crossing*, in which a neighbouring nerve is cut to provide a central stump to which the peripheral stump of the injured nerve may be directly sutured.

The present paper, from the Department of Zoology and Comparative Anatomy, Oxford, is an extensive review of the clinical and experimental literature of these procedures. The author concludes that manipulative operations have been, and are likely to remain, the most widely used methods for the repair of gaps in the peripheral nerves. There is no evidence that such methods as mobilisation and transposition have an adverse effect upon the ultimate quality of recovery. Severe degrees of nerve stretching, however, may cause damage, but the amount of stretch that may be applied to a regenerating nerve without causing damage is not known. There are indications that a stretch of about 10% of the mobilised length of the nerve may be applied without damage, but that a total stretch of as much as 30%, such as may be applied during two-stage operations, may be harmful. In gaps so extensive as to require this amount of stretch to close them, some sort of bridging is probably a preferable procedure.

In addition there are certain well-defined situations where manipulative procedures are relatively ineffective, and here bridge operations are indicated. These situations are:

(*a*) In the repair of the digital nerves (*see* Bunnell & Boyes, 1939).

(*b*) In lesions of the brachial plexus, particularly injuries to C5 and C6, where extensive mobilisation is difficult. Moreover, the difficulty of end-to-end suture in partial lesions of the cords of the plexus makes an inlay graft worthy of trial in this situation, particularly owing to the ease with which such a graft can be fixed in position with the plasma "glue" introduced by Young & Medawar (1940).

(*c*) In lesions of the peroneal nerve, particularly in repairing the very extensive gaps left after resection in traction lesions.

(*d*) In the repair of the facial nerve in the temporal canal (Ballance & Duel, 1932).

Among bridge operations the most successful are nerve grafts. Nerve flaps, *suture à distance*, and tubulisation should be discarded on the experimental evidence. Double lateral implantation is insufficiently documented to warrant any conclusion as to its value on the present evidence, and its performance is attended by considerable risk to the host nerve.

On the available evidence, autografts are the most successful type of graft. They survive, undergo Wallerian degeneration, and can conduct new fibres to the peripheral stump. Although fibres grow slightly more slowly through an autograft than through a normal peripheral stump, the difference (between 3·5 and 2 mm./day in the rabbit) is not sufficient to cause any great delay in the recovery of autografts as compared with end-to-end sutures. The rate of outgrowth is not increased by the use of pre-degenerated, as opposed to fresh, nerve as a graft. Moreover, grafts with preserved vascularisation, consisting of a pedicle taken from a neighbouring nerve, are very rapidly innervated, but the method is not to be recommended for surgical use, on account of damage to the neighbouring nerve. Fresh free autografts are the best except in certain situations (temporal canal) where predegeneration gives a graft of firmer consistency which is more easy to handle.

To allow outgrowth of all its fibres, a graft must exceed, or at least equal, the diameter of its host nerve. Thus in autografts of the thick nerves of man, cable grafts become a necessity. These grafts have never been compared experimentally with full-thickness grafts, but it is significant that the clinical cases showing recovery in autografts are those where either cable grafts, or thin grafts in thin nerves, have been used. There is evidence that necrotic zones occur in thick autografts. Thus, besides being a surgical necessity, cable grafts may possess an advantage in enabling rapid vascularisation of the whole graft to take place. The chief difficulty of these grafts is their preparation and insertion, and it is probable that many of the alleged failures of autografts in the literature have been due to faulty technique. In this instance, both the method of Elsberg (1919), and the plasma "glue" mentioned above, may be of considerable use.

Compared with the results of end-to-end suture, the introduction of an extra point of junction, where ravelling of fibres can occur, must be a point militating against the success of autografts. Too much emphasis must not be placed upon this point until it is known how far the superfluity of fibres produced during regeneration compensates for loss of fibres by deviation. However, some authors (Davis & Cleveland, 1934) have postulated a connective tissue invasion of the lower junction of long grafts, while fibres are still in the upper part of the graft, which causes considerable loss of fibres by deviation upon their arrival at the lower junction. This has been made the basis for a practice of resection and resuture of the lower junction in long grafts after the arrival of fibres, and it is claimed that this gives a juncton with fewer deviated and whorled fibres, and thus a better recovery. However, it has been shown (Sanders & Young, 1942) that the lower junction, even in long grafts, is made by the Schwann cells before the arrival of fibres, and there is no reason to suppose that connective tissue invasion interferes seriously with these pathways. Resuture of the lower junctions of autografts does not appear theoretically to be necessary.

Compared with autografts, the value of homografts is less certain. Experimentally they have been shown to unite with the host nerve, degenerate, become re-innervated, and to be followed by a recovery only a little inferior to that obtained with autografts. Clinically their record is not sufficiently complete to warrant any definite conclusions. Alcohol-fixed grafts, and all other forms of dead nerve grafts, are definitely contra-indicated by both the experimental and the clinical evidence.

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122

THE DEGENERATION AND RE-INNERVATION OF GRAFTED NERVES

by F. K. Sanders & J. Z. Young, *Journal of Anatomy*, **76**, 143–165, January 1942

In the experiments described in this paper from the Department of Zoology and Comparative Anatomy, Oxford, the efficiency of different types of nerve graft was compared by finding the distance which pain fibres had grown through the grafts after short periods (mostly 15 and 25 days) and by careful examination of the histological conditions at these times.

Autografts behave very like normal peripheral stumps. The Schwann cells of the graft survive and multiply, and the myelin breaks up and is removed by macrophages. After a delay of about 9 days at the upper junction, new fibres grow through the graft at 2·0 mm./day, and by 25 days are already medullating in it. At the lower junction there is a maximum delay of 1·7 days, the junction being made by Schwann cells independently of the presence of nerve fibres. This is so even for grafts 5 cm. long, and there is no reason to resort to resuturing a lower junction, apart from a slight tendency of grafts to shorten, which may result in bad junctions in some cases. Predegeneration of the graft does not cause it to be more rapidly penetrated by new fibres.

Homografts set up a considerable lymphocytic reaction, which may lead to partial necrosis. However, proliferation of Schwann cells and myelin break-up occurs, although the latter may be abnormal. Fibres are also able to medullate in the graft, although the rate at which homografts are penetrated by new fibres is slower and more variable than in autografts.

In *homografts stored for 7–21 days in Ringer's solution* at 2° C. the lymphocyte reaction is reduced or absent, although there is a great invasion by macrophages. Schwann cells, nevertheless, survive and proliferate, and new fibres are able

to grow into the graft. They are, however, abnormally thick and rather few in number, and the rate at which they penetrate the graft is variable, although sometimes faster than in control fresh homografts.

Heterografts of dog or rat nerve in the rabbit set up a vast cellular reaction at their edges, and do not degenerate. There is no Schwann proliferation or myelin break-up, and few new fibres enter the graft. A graft of rabbit nerve in a dog produced a very great reaction, by which most of the graft was removed.

Alcohol-fixed homografts are removed by macrophages. New fibres do not enter such a graft, although they may grow well into the bed of macrophages and fibroblasts which replaces it, and so reach the peripheral stump.

A piece of *alcohol-preserved formol-fixed spinal cord* used as a heterograft was encapsulated and attacked by giant cells. New outgrowths proceeded around but not within it.

The authors conclude that in the rabbit the behaviour of autografts provides a good basis for functional recovery. Homografts can also do so, but in some cases set up reactions, which can be reduced by previous storage of the graft. Heterografts, and grafts of dead tissue, provide for reunion of the stumps only after destruction and replacement of the graft, and are thus unlikely to be followed by a successful recovery in man.

123

THE HISTOLOGICAL CONDITION OF A NERVE AUTOGRAFT IN MAN

by H. J. Seddon, J. Z. Young, & W. Holmes, *British Journal of Surgery*, **29**, 378–384, April 1942

The purpose of this paper is to demonstrate that an autogenous nerve graft in man can function as a living bridge in peripheral nerve reconstructions. Although a certain number of successes have been recorded, the general view held by most British observers is pessimistic and it remained to be proved that the tissue bridging the gap was not merely converted into a fibrous band but remained as viable nerve elements.

The case reported here is of a man of 26, whose median nerve had been divided 10 cm. above the elbow by a bomb splinter. Three months later he was operated on, and the nerve was freed from a large amount of scar tissue. The affected portion of nerve was resected, but the ends could not be brought together without tension, and an autogenous graft of the medial cutaneous nerve of the forearm was therefore inserted and secured by a fibrin coagulum, as described by Young & Medawar (1940). Histological examination of the resected nerve tissue showed that, at the proximal end, normal nerve tissue had not been reached, and although there were some clear bundles, many others were irregularly scattered, the fibres were small and surrounded by proliferating Schwann cells and macrophages, and there was much interfascicular fibrosis. The peripheral end of the resected portion showed only a few scattered bundles and consequently neither side of the gap could be regarded as a suitable bed for the nerve graft.

No sign of recovery was detectable after six months, and in view of the unfavourable histological report on the first specimen, another operation was performed in which the graft, together with a further portion of the central and peripheral stumps of the nerve, was resected. By very extensive mobilisation and extreme flexion of the elbow, the gap was closed without tension.

Histological examination showed that the central nerve bundles had made a good junction with the graft bundles. The latter were well preserved and surrounded by fibrous tissue in which were embedded many small new bundles. The original bundles of the graft contained abundant elongated Schwann cells and had lost their myelin sheaths, but the newly formed fibres, although smaller than the old ones, showed medullation.

Only a few bundles of the peripheral stump made contact with the graft at the original operation and consequently most of the graft bundles were separated from the peripheral stump by scar tissue. The fibres that had grown through the grafts sprouted out in all directions into the junction scar. Some, however, in spite of the unfavourable circumstances, had reached the peripheral stump and were there seen as medullated nerve fibres.

The authors conclude that under suitable conditions transplanted nerves can remain alive and become directly incorporated. The conditions in this case were on the whole unfavourable, but viable graft tissue with newly formed fibres was present six months later. Better results might be expected if the local conditions were good, and if particular attention were paid to the size of the graft to ensure that its cross-section area was approximately equal to that of the nerve stumps.

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[1] [*See BMB* **117**]

124

FUNCTIONAL RECOVERY FOLLOWING NERVE GRAFTS AND OTHER TYPES OF NERVE BRIDGE

by E. Gutmann & F. K. Sanders, *Brain*, **65**, 373–409, December 1942

In this paper from the Department of Zoology and Comparative Anatomy, Oxford, the authors have made an experimental study of the degree of functional recovery following nerve grafts and other types of nerve bridge. The peroneal nerve of the rabbit was cut in the thigh and repaired by (*a*) unaided union of stumps; (*b*) end-to-end suture; (*c*) various types of nerve graft. The time of onset of motor recovery and its degree in the muscles of the small peroneus group were determined by measuring the return of reflex spreading of the toes in the way described by Gutmann (1942). Recovery of pain sensibility in the skin of the dorsum of the foot was also studied, and the histological conditions of the various grafts as late as 200 days after operation. In this way it was possible to compare the recovery produced after the various procedures more thoroughly than has previously been possible.

Eight out of eight cases of end-to-end suture recovered toe-spreading 56–85 days after operation; 8 out of 10 autografts in 51–98 days; 6 out of 7 fresh homografts in 70–125 days; 8 out of 8 homografts stored for 7, 14 or 21 days in Ringer's solution at 2° C. before insertion in 61–117 days; 2 cut of 4 dead alcohol-fixed grafts in 124 and 142 days; and 2 out of 14 unaided unions in 117 and 162 days.

After no procedure was the normal amplitude of movement restored. After recovery, end-to-end sutures and autografts resulted in the amplitude of spreading which came nearest to normality. With fresh homografts and stored homografts there was a recovery-spreading of somewhat smaller amplitude. Spreading of the least amplitude was shown by alcohol-fixed grafts and unaided unions.

Sensory recovery on the dorsum of the foot occurred with end-to-end sutures in 124 and 159 days; with an autograft at 174 days; with fresh homografts in 172–200 days; with stored homografts in 174–200 days; recovery failed to appear before 200 days with all alcohol-fixed grafts and unaided unions.

The structure of the various grafts at 200 days showed the effect of the tissue reactions which sometimes accompany the earlier stages (*see* Sanders & Young, 1942). Autografts were indistinguishable from normal peripheral stumps. Fresh homografts showed fibrotic zones and often spaces with macrophages; the extensive lymphocytic infiltration, often found in the early stages, had disappeared by 200 days. Stored homografts showed some fibrosis, but otherwise resembled normal nerve, there being no trace of the excessive macrophage invasions present in the early stages. Alcohol-fixed nerves showed evidence of destruction and replacement by the host tissues, and consisted of connective tissue masses traversed by new fibres in irregular bundles. They resembled the strand connecting the stumps in unaided unions. Nevertheless at 200 days, grafts, peripheral stumps, and the strand of tissue connecting the stumps in unaided unions all contained myelinated nerve fibres. These were more numerous in normal peripheral stumps, autografts, and Ringer-stored homografts than in fresh homografts, alcohol-fixed grafts, or unaided unions. Fibres also attained a greater diameter in autografts than in homografts, where the largest fibres were restricted to the edges of the graft. The smallest fibre-size was attained in alcohol-fixed grafts. In the two autografts and one homograft in which recovery

failed, the grafts were reduced in diameter, contained many macrophages, and only a few thin nerve fibres.

This study of functional recovery following nerve grafts shows that autografts can survive, become re-innervated, and be followed by as rapid and complete a recovery as after end-to-end suture. Homografts can also be followed by recovery, but this occurs a little later than in autografts and is not so complete—presumably owing to adverse tissue reactions. Previous storage of the graft, which reduces these reactions, promotes a more complete recovery, but does not make it occur significantly earlier. Alcohol-fixed grafts are replaced by the tissues of the host, and are followed by very late and poor recoveries, comparable to those obtained after the unaided union of stumps.

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125

THE CHEMICAL INHIBITION OF FIBRE REGENERATION AND NEUROMA FORMATION IN PERIPHERAL NERVES

by L. Guttmann & P. B. Medawar, *Journal of Neurology and Psychiatry*, **5**, 130–141, July & October 1942

Acute pain in amputation stumps and peripheral nerve injuries is frequently associated with neuroma formation by the central stumps of the severed nerves. Pain is often relieved by excising the neuroma and taking certain methods to prevent its recurrence. In the past methods have been used which fall roughly into two classes: (i) *surgical and mechanical methods*, involving diversion of the affected stump into muscle or bone, or crushing, ligature, or closure of the end of the stump; (ii) *physical or chemical methods*, in which a length of nerve is destroyed by freezing or cauterisation, or by the injection of substances designed to prevent regeneration.

The authors of the present paper strongly criticise surgical and mechanical methods, on the ground that, while they may prevent escape of nerve fibres from the cut stump, they do not prevent the neuroma formation which is thought to be the cause of pain. A similar criticism of the more radical of these procedures was made by Huber & Lewis (1920).

With regard to chemical methods, the authors report a series of experiments, made in the Department of Zoology and Comparative Anatomy at Oxford, in which they have investigated the effect on neuroma formation of the injection of a number of substances into the tibial nerve of the rabbit. The substances used fall roughly into two classes: (*a*) *fixatives*, i.e. chemical coagulants of protoplasm; and (*b*) various *non-fixatives* which have a specific action, such as the inhibition of amœboid movement or the stimulation of fibroblast proliferation.

The results of these experiments showed conclusively that fixatives as a class were superior inhibitors of neuroma formation to the other substances. Formaldehyde, at concentrations of 20% and over, prevented the formation of either bulbs or adhesions for at least a year after injection. Aqueous gentian violet (1%) was equally effective. Alcohol was effective only for periods of less than 2 months, while other fixatives, such as chromic acid and mercuric chloride, occupied an intermediate position.

Histological investigations showed that the action of the successful inhibitors was a sort of "chemical defence in depth." The effect was due to the maintenance in the injected portion of nerve of an environment which is permeable, but only just permeable, to regenerating nerve fibres. The presence of many nerve fibres was shown to be necessary to the formation of a neuroma. Thus the fixed nerve was only very slowly penetrated by them, and the formation of a neuroma was indefinitely delayed.

The paper concludes with a discussion of the application of the technique to the injection of human nerves.

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126

LOCAL APPLICATION OF SULPHANILAMIDE TO PERIPHERAL NERVES

by W. Holmes & P. B. Medawar, *Lancet*, **2**, 334–335, 19/9/42

In this paper from the Department of Zoology and Comparative Anatomy, Oxford, the authors report a study of the effect of sulphanilamide applied around the sciatic nerve of the rabbit. The nerve can withstand as much as 1 g. of the drug packed into the thigh, but with 2 g. there is interruption of the nerve fibres and complete Wallerian degeneration. The test is of course a severe one. The operation site is clean and bloodless. However, they conclude that, since sulphanilamide is sufficiently soluble to exert a damaging effect on nerve, it should be used with caution at operations in which peripheral nerve trunks are exposed.

TRACTION INJURIES OF NERVES

127

TRACTION INJURIES TO THE LATERAL POPLITEAL NERVE AND TRACTION INJURIES TO PERIPHERAL NERVES AFTER SUTURE

by W. B. Highet & W. Holmes, *British Journal of Surgery*, **30**, 212–233, January 1943

In this paper from the Nuffield Department of Orthopædic Surgery and the Department of Zoology and Comparative Anatomy, Oxford, the authors have made a study of traction injuries and the similar conditions which are produced by attempts to stretch nerves too strongly after resection and suture. Eight cases of traction injury to the lateral popliteal nerve were treated surgically, and the lesions were examined histologically.

They found that the traction lesion is characterised by much more extensive damage to the nerve-trunk than is found after injury by incision, laceration, or gunshot wound. The pathological changes in the nerve extend far above the site of obvious damage, in the form of fibre degeneration, intraneural fibrosis, and vascular abnormality. The connective tissue sheaths of the nerve undergo rupture to a varying degree; thus the nerve may be completely divided, or bear a fusiform neuroma, or show macroscopical continuity. Spontaneous recovery did not take place even in cases in which nervous tissue was continuous throughout the lesion. Regenerating nerve-fibres succeeded in crossing the lesion, but they remained small in diameter and most of them failed to become myelinated. In three cases end-to-end suture was performed after an extensive resection of the lesion: closure of the gap was obtained by extensive mobilisation of the nerve and flexion of the knee. No recovery took place in these cases. In one case in which a less extensive resection was necessary a good recovery is in progress. A further exploration of the nerves which failed to show recovery after suture was carried out. Histological examination showed pathological changes similar to those following the original lesion, but even more severe and extensive.

The authors conclude that failure of recovery after extensive resection and suture may be due to injury inflicted on the nerve during post-operative extension of the joint.

128

THE EFFECTS OF STRETCHING NERVES AFTER SUTURE

by W. B. Highet & F. K. Sanders, *British Journal of Surgery*, **30**, 355–369, April 1943

This paper from the Nuffield Department of Orthopædic Surgery, and the Department of Zoology and Comparative Anatomy, Oxford, reports a series of experiments on nerve stretching made as a corollary to the clinical work of Highet & Holmes (1943).

Gaps in the external popliteal nerves of dogs, following extensive resection of the nerve in the thigh, were closed by flexion of the knee and suture of the stumps with the limb in this position. After keeping the knee flexed for 14 days in a plaster cast, the nerve was stretched by extending the knee either (*a*) rapidly, by the animal's own movements, or (*b*) gradually, with a "turnbuckle" plaster [a pair of casts enclosing a limb above and below a joint and connected by a screw. By turning the screw, the casts are pushed apart and

the joint is forcibly extended]. The site and extent of nerve stretching was determined by the changes in position of a line of silver clips placed along the nerve at operation, and photographed by X-ray before and after stretching.

In the normal animal some elongation of the nerve over its whole length from the sciatic plexus to its entry into the shank musculature accompanies extension of the knee, but by far the greatest part of the increase in the length of the course of the nerve during knee extension in the normal animal occurs by straightening out of the tortuosity of the nerve.

When gaps have been closed by flexion of the knee the extra distance is made up by elongation of the nerve. Straightening out of tortuosity plays only a minor part. The elongation thus produced is not distributed uniformly along the length of nerve. Scar tissue formed about the suture line binds the nerve to its bed, and disproportionate stretching of the peripheral stump occurs. After such stretching the nerve returns to its original length with each subsequent flexion of the knee. Permanent elongation of the nerve does not take place in the first 35 days after operation.

The above procedure produced histological damage of the following kinds: (i) extensive, abnormal, degeneration in the central stump, (ii) where the suture line is not bound by scar tissue, separation of the stumps can take place, (iii) rupture of Schwann tubes where stretching is at all severe, (iv) extensive œdema and fibrosis both without and within nerve bundles, causing considerable disruption of the pattern of the nerve. All these factors tend to reduce the chances of a recovery of a good quality.

Rapid nerve stretching did not cause any more damage than slow stretching, except, perhaps, in so far as separation at the suture line occurred more frequently.

From the results of these experiments the authors conclude that there is probably an upper limit to the size of gap that can be overcome by post-operative nerve stretching in man, and be compatible with recovery.

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FACTORS AFFECTING RECOVERY AFTER NERVE INJURY

[In spite of the great amount of material available from the study of nerve injuries in man, there is still very little thoroughly reliable information as to the factors which influence the degree of recovery. Cases have generally followed war wounds or accidents: the nerve has been injured over varying lengths; the blood supply has been damaged, or there has been sepsis; surgical treatment has varied from case to case, and these and many other variables have combined to make comparison of clinical cases difficult.

In the two papers summarised below, Drs. E. Gutmann and L. Guttmann, working in the Department of Zoology and Comparative Anatomy at Oxford, have attempted to define more closely the various factors which influence motor and sensory recovery after nerve injuries. They have done this by means of animal experiments in which all those variables which are the disadvantage of clinical material can be separately and accurately controlled.]

129

FACTORS AFFECTING RECOVERY OF MOTOR FUNCTION AFTER NERVE LESIONS

by E. Gutmann, *Journal of Neurology and Psychiatry*, **5**, 81–91, July & October 1942

In this paper the author has attempted to define the influence on motor recovery of (i) the nature of the lesion, (ii) its level, (iii) interference with blood supply of the limb, (iv) age of the subject, (v) infection, and (vi) delay of suture.

The animals used were rabbits and the peroneal nerve was interrupted at an initial operation in one of four ways: (1) by crushing at a single point with fine forceps; (2) by severance followed by suture with either cockerel plasma or fine white silk stitches; (3) by crushing with broad forceps over a length of 4 cm.

Motor recovery was followed by almost daily examination of the toe-spreading reflex of the hind limb, a function performed by muscles innervated by the peroneal nerve. Other criteria of muscle recovery were also examined, namely: (*a*) the response to electrical stimulation of the nerve, (*b*) the direct excitability of the muscle, (*c*) the circumference of the limb in the region of the denervated muscles, (*d*) the weight of the muscles, (*e*) the disappearance of fibrillation.

After crushing the peroneal nerve at the knee, nerve fibres first return to the muscle after about 10 days, contraction on stimulation of the nerve after 18–20 days, first reflex spreading of the toes after about 25 days. Full amplitude of spreading is not achieved until 33 days, and for a time spreading may exceed the normal amplitude, although it eventually regains normality. The circumference of the limb with denervated muscles begins to increase, and the threshold of these muscles to direct stimulation to decrease, before reflex spreading, and sometimes before even electrical excitability via the nerve appears. Fibrillations continue in the muscle about 2 weeks after the first appearance of reflex function, but the normal weight of the muscles is not regained until at least 12 weeks after the first reflex spreading.

It was also found after crushing the nerve that when the lesion is more distant there is a longer delay between arrival of fibres at the muscle and the first occurrence of contraction on stimulating the nerve. Moreover the time between the appearance of reflex function and its completion is greater after more distant than after near lesions. The rate of advance of regeneration, however, is not slower with more distant lesions. It has a value of $2{\cdot}77 \pm 0{\cdot}09$ mm./day after a latent period at the lesion of $18{\cdot}2$ days.

The author found that after severance and suture all the processes of recovery are slower than after crushing the nerve. The rate of advance of regeneration is $1{\cdot}69 \pm 0{\cdot}34$ mm./day with a latent period of $27{\cdot}7$ days. The delay between arrival of fibres and the return of reflex function is greater than after crushing. After the first reappearance of reflex spreading there is only a gradual increase in amplitude, and a normal amplitude is never attained.

Recovery after crushing the nerve over a length of 4 cm. is later and less complete than after a local crush. Ligature of the popliteal artery and vein does not delay recovery, and infection does not delay recovery unless it affects the nerve itself. Age, however, markedly affects the rate of recovery, which occurs much earlier in young animals.

Cross-unions of the tibial and peroneal nerves are also followed by a recovery of toe-spreading, and this type of union has been used to study the effect of delay of suture on recovery. Delay of suture reduces the degree of recovery and retards its onset, but the effect is not marked unless the delay exceeds 6 months.

130

FACTORS AFFECTING RECOVERY OF SENSORY FUNCTION AFTER NERVE LESIONS

by E. Gutmann & L. Guttmann, *Journal of Neurology and Psychiatry*, **5**, 117–129, July & October 1942

The experiments described in this paper were undertaken at the same time as those on motor recovery summarised above, and had three main objects: first, to delimit the maximal and autonomous areas of the skin served by various nerves in the hind limb of the rabbit; secondly, to show the manner in which shrinkage of the insensitive area left after denervation takes place, and the parts played in this shrinkage by (*a*) recovery in the zone of overlap between the interrupted and its adjacent nerves, (*b*) recovery in the autonomous zone of the interrupted nerve; and thirdly, to show how recovery is affected by such factors as the nature of the lesion, its distance from the skin, age of the animal, and infection.

The skin areas innervated by the peroneal, tibial, sural, saphenous, and postero-lateral cutaneous nerves are described. In these cases the maximal zone was determined by the area of remaining sensibility after section of all the adjacent nerves, leaving the nerve in question intact. The autonomous zone was determined by the area of analgesia left some time after isolated section of the nerve in question, the prevention of regeneration from the central stump by extensive resection, and by waiting for the process of recovery in overlap zones to run its course.

From a study of the extent of the analgesic zones found at various times after these two types of operation the authors conclude that recovery of analgesic area is a complex process comprising three main phases: (i) recovery in zones of overlap by the progressive resumption of function by fibres of adjacent nerves; (ii) extension of these fibres into the denervated area [a histological investigation of this phenomenon has been made by Weddell, Guttmann & Gutmann, 1942]; (iii) regeneration of the interrupted nerve.

The first process, recovery in overlap zones, is generally complete 2 to 4 weeks after interruption of the nerve in adult animals, but occurs within a few days of operation in young animals. It is peculiarly susceptible to various factors such as local damage to the skin supplied by adjacent nerves, transient block of these nerves as a result of operation, and all processes such as infection, sores, narcosis, and old age.

The third process, which comprises recovery in the autonomous zone, and is due to regeneration, proceeds in general in a downward direction. In large areas recovery often advances faster at the edges than in the centre, so that the analgesic area shrinks concentrically. This pattern of recovery, i.e. centrifugal advance and concentric shrinkage, was observed in all the nerves examined.

The authors found that the nature of the lesion profoundly affects the time and degree of recovery. After suturing the nerve the recovery was slower, less regular, and definitely of an inferior degree to that obtained after simply crushing the nerve at a single point. Crushing the nerve over a length of 4 cm. was also followed by recovery inferior to that after a single crush.

The rates of advance of regeneration also were different. After crushing, the rate of advance was 3·35 mm./day, with a latent period of 22 days; after suturing the rate was 2·46 mm./day, with a latent period of 40 days. Greater variability after suturing makes this second estimate less reliable.

The rate of advance of the margin of algesia in the autonomous zone of the peroneal nerve after crushing at various levels was found to be $1{\cdot}98 \pm 0{\cdot}09$ mm./day. After suturing it was $1{\cdot}57 \pm 0{\cdot}15$ mm./day. After crushing the rate was higher when the nerve was crushed at the ankle than when it was crushed in the thigh.

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THE ACTUAL PROCESSES OF NERVE REPAIR

131

NERVE REGENERATION AFTER IMMEDIATE AND DELAYED SUTURE

by W. Holmes & J. Z. Young, *Journal of Anatomy*, **77**, 63–96, October 1942

Studies of the histology of nervous regeneration have previously been restricted to the period following a primary suture (*see* Cajal, 1928), whereas in man suture is often much delayed.

In this paper from the Department of Zoology and Comparative Anatomy, Oxford, the authors have re-investigated the histological aspects of regeneration in nerves, laying special emphasis on the process of re-innervation of stumps which have been allowed to degenerate for a long time. They emphasise that during degeneration the pattern of a nerve is maintained by the endoneurium and neurilemma, a Schwann tube being formed in place of each original fibre. Each tube gradually contracts, finally reaching about half the diameter of the original fibre. Macrophages enter these tubes and remove the remains of axons and myelin. They are abundant from about the 8th to the 25th day and thereafter disappear gradually, some persisting for a year or more. The protoplasm of the Schwann cells increases in amount and after nuclear division elongated cells are found, lying side by side in the larger tubes. In the early stages the Schwann cells do not entirely fill the tubes. They gradually replace the macrophages and when the tube is fully contracted its whole cross-section is filled with fibrillar Schwann protoplasm, the nuclei becoming extremely elongated. Such Schwann cells may easily be mistaken for nerve fibres, especially when stained with silver. In the early stages the Schwann cells probably move within the tubes. Certainly they emerge at the end of the peripheral stump and are the main agent for leading fibres back into the old tubes. Growth and mitotic division take place in the Schwann tissue which has migrated from the peripheral stump. The tip of the outgrowth was found to have reached to an average distance of 1·4 mm. in 15 days, and 2·2 mm. in 25 days. But the outgrowth does not continue progressively if the stump is left un-innervated.

Normal nerve fibres in the walls of the intraneural blood-vessels usually send out collaterals into the nerve tissue of isolated degenerated stumps. They remain very small and are rarely medullated, but are sufficient to produce a reflex response on stimulation and an outgrowth of nerve fibres from the peripheral end if the stump be again cut. The endoneurium and perineurium of a long-degenerated stump become moderately but not excessively collagenised. The diameter of the whole nerve may decrease by as much as one-half.

When new fibres grow into a freshly cut peripheral stump they run along the inner walls of the Schwann tubes. Where possible they grow along the surfaces of Schwann cells, but do not at first lie within them. As many as twenty fibres may enter a single tube. One or more, rarely several, of these increase in diameter, and become surrounded by Schwann cell protoplasm and medullated. The others remain for a while around the periphery of the tube and presumably they ultimately atrophy.

The power of a central stump to send out new fibres is not reduced if it be severed a second time and then sutured, either within a week or after an interval as long as a year. The power of a peripheral stump to put out Schwann cells is greatest if it be cut a second time some 2–3 weeks after its first severance. Thereafter this power declines, and unions made with peripheral stumps degenerated for more than 100 days are often unsatisfactory. However, once within a peripheral stump which has been degenerated for a long time, fibres may proceed as rapidly as into a freshly cut stump. Fewer fibres penetrate into a stump which has been degenerated for a long time than into a freshly cut one. Medullation proceeds much more slowly after delayed suture. There are thus various other factors, in addition to atrophy of the end-organs, which are likely to reduce the effectiveness of recovery where suture is made after a long delay.

The authors conclude that the processes of union of stumps and the regeneration of a new functionally efficient stretch of nerve are less satisfactory after the longer periods of degeneration. Delay in suturing for 1 or 2 months does not prejudice the chances of recovery, and may even improve them; longer delays, especially those greater than 5 or 6 months, produce conditions which at least are liable to retard recovery, and may permanently prevent its completion.

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132

THE OUTWANDERING OF CELLS IN TISSUE CULTURES OF NERVES UNDERGOING WALLERIAN DEGENERATION

by M. Abercrombie & M. L. Johnson, *Journal of Experimental Biology*, **19**, 266–283, December 1942

These authors, working in the Department of Anatomy and Zoology, Birmingham, have investigated the effect of various periods of degeneration on the power of outgrowth of the Schwann cells which are so important for making the union between nerve stumps. They used the technique of tissue culture. Ingebrigtsen (1916) first showed that these cells emerge from a piece of nerve explanted into a culture medium in vitro. This growth takes place only if the piece of nerve which is explanted has been severed some time previously.

The present authors were able to measure the degree of activity at various times after severance. They found that, in the peripheral stump, Schwann cell activity begins on the 2nd day after cutting, and from the 4th day rises rapidly to

a peak at the 19th–25th day. It then falls quickly up to about the 60th day and afterwards more slowly. Activity is still appreciable more than a year after cutting. These changes of activity according to the time of degeneration are shown by thigh, knee and shank regions of the peripheral stump. The knee region, and the shank (which is 8 cm. distal to the initial cut) are more active than the thigh region, especially in the early days of degeneration.

In the central stump, activity is at first confined to a few mm. immediately adjacent to the cut. From the 2nd to the 4th day after cutting, the central stump is more active than the peripheral stump, but thereafter it is much less active. Its maximum activity never reaches more than 10 % of the maximum activity of the peripheral stump. Activity is still appreciable more than a year after the cut was made. The more proximal part of the central stump, at first inactive, begins to show slight Schwann cell activity after 29 days and is still active after more than a year.

Since Schwann cells probably play an important part in forming the junction when severed nerves are repaired, this work indicates the optimum from this point of view for making grafts or sutures. The experiments indicate that the Schwann cells will be more active in joining together two nerve stumps if the nerve or nerve graft is left a few (say 10–20) days to degenerate before making the repair; and that (in the rabbit) the optimum time for suture is passed 25 days after the nerve is cut.

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133

RECOVERY OF FIBRE NUMBERS AND DIAMETERS IN THE REGENERATION OF PERIPHERAL NERVES

by E. Gutmann & F. K. Sanders, *Journal of Physiology*, **101**, 489–518, March 1943

The process of regeneration of a nerve can be divided into two contiguous phases: (i) that of *outgrowth*, which has as its result the arrival and connexion of fresh axons with the periphery, and (ii) that of *reconstitution*, whereby the numbers, diameters, and medullation of the fibres are restored. This latter phase of regeneration has received little attention until now. The authors of this paper, from the Department of Zoology and Comparative Anatomy, Oxford, have investigated the process of reconstitution by means of counts and measurement of the fibres in the peroneal nerve of the rabbit at intervals after either crushing the nerve, or cutting and repairing it by suture or nerve graft.

The peroneal nerve normally contains 6000–9000 medullated nerve fibres, varying in size from 1 to 20 μ. The frequency distribution of fibre diameters is a bimodal one, with peaks at 2–3 and 13–14 μ. Only after crushing the nerve were the normal number and distribution of the fibres in the peripheral stump eventually restored. Reconstitution was complete at about 300 days after operation. As late as one year after suture, or 200 days after nerve grafting, neither the number nor the pattern of fibres was restored.

It is of interest that the fibres in the central stump above the lesion were found to shrink during the early stages of reconstitution, as though they were being depleted by an outflow.

134

THE RATE OF REGENERATION OF NERVE

by E. Gutmann, L. Guttmann, P. B. Medawar, & J. Z. Young, *Journal of Experimental Biology*, **19**, 14–44, May 1942

In this paper from the Department of Zoology and Comparative Anatomy, Oxford, the authors report the results of measuring the rate of advance of regeneration along nerves in the rabbit in five different ways. Not all the methods gave the same result, and the authors conclude that the concept " rate of regeneration " is far from being simple. When the rate of advance of the growing axon tips is studied, a higher rate is recorded than when the times necessary for functional recovery are considered. In the latter case, the experiment measures the rate of advance, not of the tips of the regenerating axons, but of completed nerve fibres, able to function.

The factors determining the time which elapses between suture and recovery are therefore: (i) the " scar delay," which includes the time necessary for the fibres to undergo retrograde degeneration, branching, and the relatively slow process of growth across the suture scar; (ii) the rate of progress down the nerve of a process of " functional completion," which lags behind the more rapidly advancing axon tips.

The " scar delay " is nearly constant after all well-made sutures (7·3 days). After crushing the nerve it is only slightly shorter (5·2 days). There is a further delay before the process of functional completion begins to advance down the nerve, so that there is a total latent period of 36 days after suture and 20 days after crushing.

The rate of advance of the axon tips was determined by finding the furthest point from the lesion at which nociceptive reflexes could be elicited by pinching the nerve. This rate is not significantly different in the three divisions of the sciatic nerve, or after interrupting the nerve at different distances from the nerve-cell bodies. After suture it has a value of 3·5 and after crushing of 4·4 mm./day.

The rate of advance of functional completion of nerve fibres was measured by making lesions at various levels and studying: (*a*) the time necessary for return of response to nociceptive stimuli to a given point on the skin, and (*b*) the time for recovery of a given motor function, namely, spreading of the toes. Both methods gave rates of 2·0 mm./day after suturing, 3·0 mm./day after crushing.

Comparison of the times of recovery of muscles at varying distances from a lesion gives an estimated rate of advance of functional completion of 2·2 mm./day after crushing a nerve, but this method is only approximate in the rabbit.

Analgesic areas on the foot shrink during recovery at a rate of 2·1 mm./day after crushing and 1·6 mm./day after suture.

In rabbits one month old, the rate of advance of the axon tips is not greatly different from that in adults, but the scar delay is less, and functional completion proceeds more rapidly.

It is concluded, from a study of the experimental results and from published data, that the process of functional completion proceeds down the nerve faster than the accepted 1 mm./day both in experimental animals and in man.

[*Until recently, knowledge of the histology of nerve degeneration and regeneration was largely based on the changes which occur in nerve trunks, and the cutaneous nerve plexuses had received relatively little attention. The series of papers reviewed below* (*BMB* **135–138**) *gives an account of recent advances in this field. They are mainly based upon a study of total preparations of large pieces of skin, stained intravitally with methylene blue. The work was done in the Departments of Human Anatomy and of Zoology and Comparative Anatomy, Oxford.*]

135

THE EARLY STAGES IN THE DEGENERATION OF CUTANEOUS NERVE FIBRES

by G. Weddell & P. Glees, *Journal of Anatomy*, **76**, 65–93, October 1941

Weddell (1941) gave a descriptive account of the normal innervation of the skin of the rabbit's ear, and the present paper continues with a description of the changes which occur in the cutaneous nerve plexuses between 12 and 336 hours after nerve section. The changes follow the pattern generally accepted for nerve trunks, although they differ from them in certain particulars.

After nerve section the axons were found to swell up and disintegrate, the last portions to be affected being in the region of the nodes of Ranvier. Disintegration was most rapid in the non-medullated axons, and proceeded relatively more slowly in medullated fibres, the slowest fibres of all to degenerate being those of the greatest diameter. However, some of the largest fibres showed precocious degeneration, and there were resistant fibres throughout the range of sizes.

Degeneration of myelin followed its typical course. First of all a reticular network appeared throughout the myelin sheath, followed by a break-up of the myelin into droplets of various sizes, which form the so-called " ellipsoids," or

"digestive chambers." These are gradually resorbed, and by 336 hours after nerve section not one remains in the cutaneous plexus.

Between 96 and 168 hours after nerve section the Schwann cells of the cutaneous nerve plexus proliferate and come to surround the digestive chambers. By 336 hours degeneration is complete, and each nerve fibre is replaced by its connective-tissue sheath containing strands of Schwann protoplasm with elongated nuclei.

The authors could find no evidence of the supposed phagocytosis of myelin remains by Schwann cells.

In normal skin from both rabbit and man a certain number of degenerating fibres were found. These were more common in regions which are constantly subjected to minor traumata, such as the pressure point of the elbow. The authors conclude that the nerve fibres in such regions, like the lymph capillaries, are probably in constant flux, a cycle of degeneration and regeneration constantly taking place and accompanying minor irritative changes.

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136

LOCAL EXTENSION OF NERVE FIBRES INTO DENERVATED AREAS OF SKIN

by G. Weddell, L. Guttmann, & E. Gutmann, *Journal of Neurology and Psychiatry*, **4**, 206–225, July & October 1941

Pollock (1920) found clinically that the areas of sensory loss after nerve injuries can shrink circumferentially before any regeneration can have taken place from the central stump. The present authors made an experimental investigation of this phenomenon in rabbits.

In a series of animals the sural nerve (supplying a boot-shaped area on the outer aspect of the heel) was divided on one side and resected to avoid re-innervation of the peripheral stump. On the other side the tibial and peroneal nerves were divided, the sural nerve being left intact. The changes in extent of the skin areas left analgesic after these operations were mapped by both pinprick and faradic stimuli, and the skin of the region was removed at intervals from different animals, stained with methylene blue, and mounted as a total preparation.

The area of analgesia was always found to be more extensive immediately after nerve section than at later stages. Sensibility in the recovered zone was restored by two processes: (i) by re-adjustment of the function of fibres in the zone of overlap between the distribution of the cut nerve and neighbouring cutaneous nerves, (ii) by local extension of the areas innervated by nerves adjacent to the cut nerve, due to growth of new fibres through the cutaneous nerve plexuses.

The clinical terms *autonomous*, *maximal*, and *intermediate* zones, applied to the overlapping distribution of cutaneous nerves, have thus a dynamic as opposed to a static anatomical significance, for directly after nerve section, processes begin which alter the extent of these zones.

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137

AXONAL REGENERATION IN THE CUTANEOUS NERVE PLEXUSES

by G. Weddell, *Journal of Anatomy*, **77**, 49–62, October 1942

In this paper the methylene-blue technique was used to analyse the pattern of regeneration of cutaneous nerve fibres, and to correlate the results of sensory tests with the histology of regeneration. Skin was removed from the ears of rabbits at intervals of up to 12 months after the main dorsal ear nerve had been interrupted by crushing or by severance. The area of analgesia to pin-prick and to approximately threshold faradic stimuli was plotted at intervals during regeneration, and finally just before removal of the skin.

After nerve interruption there was an initial small, slow diminution of the area of sensory loss before regeneration of the fibres of the interrupted nerve actually took place. This went on for about 14 days after crushing, or for up to 4 weeks after nerve severance, and was found to be partly the result of the sprouting of fibres from neighbouring normal nerves. This confirmed the conclusion reached in an earlier paper (Weddell, Guttmann, & Gutmann, 1941). With the beginning of true regeneration, the rate of advance of the border of analgesia increased considerably, and proceeded until the whole area of analgesia recovered its sensibility.

Histologically, nerve fibres were found first to cross the scar, each fibre which succeeded in crossing throwing out a number of collaterals, and then to advance along the original main nerve fasciculi beneath the skin. After these had become re-innervated the nerve fibres pursued a tortuous course through the cutaneous nerve plexuses towards the surface of the skin, following the Schwann cell pathways which retained the pattern of the plexuses of the normal ear. The growing fibres lay at first upon the surface of the Schwann cytoplasm. Later, as the fibres matured, they became enclosed within it. As the fibres increased in diameter many of their collaterals underwent degeneration. More persistent collaterals were found after nerve section than after crushing.

The margin of regeneration as indicated histologically was usually found to be about 5 mm. in advance of the border from which the first nociceptive responses could be elicited. The author considers this discrepancy to be due to the following factors: (i) that the finest growing tips of the nerve fibres are not sufficiently mature, and are situated too far below the surface of the skin to initiate and conduct impulses in response to nociceptive stimuli; (ii) that fibres in advance of the margin of algesia, even when mature, are too few in number to give rise to a reaction on the part of the animal.

The author also found that there was a zone at the border of algesia where thresholds were raised (i.e. more random pricks, or a stronger faradic stimulus, were required to elicit a response). In such a zone many hair follicles are supplied by single nerve fibres, and the nerve nets beneath the epithelium are isolated and do not form an interdigitating series as in a normal ear. Regeneration in this zone is not yet complete.

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[1] [*See BMB* **136**]

138

OBSERVATIONS ON THE STRUCTURE OF THE CONNECTIVE TISSUE SHEATHS OF CUTANEOUS NERVES

by P. Glees, *Journal of Anatomy*, **77**, 154–159, January 1943

In this paper the author describes the structure of the collagenous enveloping sheaths of the fibres in the cutaneous nerve plexuses. Individual cutaneous bundles are surrounded by a *perineurium* consisting of longitudinal and oblique collagen fibres, the latter forming a double spiral. Each fibre has in addition an *endoneural sheath*, which consists of both longitudinal and oblique spirally arranged collagen fibres on the larger, and of longitudinal collagen fibres only on the smaller nerve fibres. Each nerve fibre is thus enclosed by a collagenous tube running all the way to its end-organ.

Following denervation, the perineurium and the endoneural tubes, which are kept distended by the hypertrophied Schwann cells, preserve the old pattern of innervation. The new nerve fibres grow down into the old endoneural tubes, and are thus forced to repeat the old pattern of ramification.

THE BLOOD VESSELS OF PERIPHERAL NERVES

139

THE BLOOD SUPPLY OF NERVES

I. Historical Review.

II. The effects of the exclusion of its regional sources of supply on the sciatic nerve of the rabbit.

by W. E. Adams, *Journal of Anatomy*, **76**, 323–341 & **77**, 243–250, July 1942 & April 1943

It is sometimes stated that little or nothing is known about the anatomical and physiological aspects of the vascularisation of nerves. The present paper, from the Anatomy

Department, Leeds University, shows that this view is erroneous. The author has collected, from scattered and often relatively inaccessible references, a great deal of information on the distribution of the *vasa nervorum*, and the physiological effects of interference with blood supply, producing a summary which is especially valuable.

Generally speaking the blood supply of a nerve is derived from regional vessels which also contribute to a longitudinal pathway along the nerve. The ganglia associated with the nerves receive a similar, but even richer, blood supply.

Experimental evidence indicates that cessation of blood-supply to any part of a nerve induces a complete nerve block. The large rapidly conducting fibres are the first to be affected, but the changes are reversible, and restoration of the circulation restores the capacity of the nerves to conduct, initiating at first exaggerated responses—the familiar "pins and needles." There is no evidence that other subjective phenomena, such as pain and vertigo, can result from ischæmia.

The second paper contains the results of an attempt to produce degeneration of the sciatic nerve of the rabbit experimentally by ligation of one or more of its regional sources of vascular supply. Ligation of the inferior gluteal artery alone produced no degeneration or other obvious histological change in the nerve in 8 experiments. In a further 12 experiments the effect of ligating all the vessels in the thigh which supply the sciatic nerve was investigated. In 10 cases either no degeneration, or degeneration of an insignificant degree, took place. In the remaining 2 cases extensive degeneration occurred, but it was not certain whether this could be attributed to manipulation of the nerve, or to some variation in the intrinsic vascular pattern in these cases.

The author concludes that severe disturbance is unlikely to follow such surgical procedures as the mobilisation of nerves, where long stretches of nerve are freed from surrounding tissue, and thus are cut off from their regional sources of vascular supply.

REGENERATION IN THE CENTRAL NERVOUS SYSTEM

140

THE PROBLEM OF NEURONAL REGENERATION IN THE CENTRAL NERVOUS SYSTEM

I. The influence of spinal ganglia and nerve fragments grafted into the brain.

II. The insertion of peripheral nerve stumps into the brain.

by W. E. Le Gros Clark, *Journal of Anatomy*, **77**, 20–48 & 251–259, October 1942 & April 1943

While the great regenerative power of peripheral nerve axons has become a commonplace of neurology, there is still some doubt whether the axons of the central nervous system possess a similar power. The experiments described in these two papers from the Department of Human Anatomy, Oxford, were undertaken in order to determine the limits of the regenerative processes which may occur in the brain. Those described in the first paper were in essence a repetition of the experiments of Tello (1911), which appeared to demonstrate not only that neurones of the central nervous system have a capacity for regeneration similar to those of peripheral nerves, but that this capacity is stimulated to expression by neurotropic substances elaborated in degenerating nerves.

Pieces of the peripheral stump of sciatic nerves degenerated for 10–14 days were placed in the brain of another animal immediately dorsal to the corpus callosum, extending transversely between the hemispheres. In some experiments spinal ganglia were grafted into the brain alongside the nerve fragments. Only 3 out of 13 pieces of grafted nerve were found to contain a very few nerve fibres 13 to 20 days after implantation. In two of the cases the nerve fibres were traced to fasciculi accompanying newly formed blood vessels. In no case could the fibres be traced to the host brain, although the Schwann tissue of the graft was in continuity with the tissues of the host brain, and there was no fibrous barrier. In some experiments, however, the fibres in the white matter were found disposed in fasciculi oriented towards the graft, exactly as Tello observed. This appearance was found to result from a traction effect exerted on the host tissue by the grafted tissue and the cellular reaction which accompanies its implantation.

The cells of grafted spinal ganglia showed great regenerative activity, and fibres grew from them into the zone of infiltration separating the graft and the host brain.

All the grafts of the above series of experiments were homografts, and it is possible that the cellular reaction to the foreign tissue adversely affected the result. In the second series the peripheral stump of the facial nerve was inserted directly into the brain, which combined the advantages of an autograft with retention of the vascular supply of the graft. Proliferated Schwann tissue grew out into the tissues of the brain, and was occasionally accompanied by nerve fibres which grew down the implanted nerve from the cut central stump outside the skull. A few regenerating fibres were also found whose origin was the blood vessels. No evidence was found of regeneration of the cerebral neurons, although these came into the closest contact with Schwann cells and regenerating peripheral fibres.

The author concludes that the intrinsic fibres of the brain have little or no regenerative capacity.

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OBSERVATIONS ON DENERVATED MUSCLE

141

EFFECT OF ELECTROTHERAPY ON DENERVATED MUSCLES IN RABBITS

by E. Gutmann & L. Guttmann, *Lancet*, **1**, 169–170, 7/2/42

The authors recall that it is just over 100 years ago that John Reid (1841) published in Edinburgh a paper on the relations between muscular contractility and the nervous system, in which he described for the first time the beneficial effect of a galvanic current on denervated muscles. Since then, opinions on the value of electrotherapy in the treatment of peripheral nerve lesions have varied greatly, and available experimental results do not appear to be conclusive.

The present paper reports a study carried out in the Department of Zoology and Comparative Anatomy, and the Nuffield Department of Surgery at Oxford, on the effect of the galvanic current on denervated muscles in the rabbit, with particular attention to: atrophy of the denervated muscles; electrical excitability and contractility; time and quality of recovery of function. The muscles used were those in the group supplied by the peroneal nerve, which was crushed in both limbs by fine forceps approximately 80 mm. from its entry into the *peroneus longus* muscle.

In all cases systematic exercise by galvanic current was carried out daily on one limb for 15–20 minutes, at a current strength of 4–6 milliamperes by means of a dry battery apparatus of 120 volts. The other limb was left untreated as a control. During the first 2 weeks after operation, electrotherapy did not prevent atrophy, but in the subsequent weeks the decrease in the circumference on the treated side was slower in all animals and in no case was the ultimate atrophy so great as on the untreated side. In all cases the exercise accelerated the recovery from atrophy, after the muscles had become re-innervated, the treated side attaining its normal measurement more quickly than the untreated side.

During the treatment individual denervated muscles were subjected to faradic stimulation via the skin and it was found that although both the galvanically exercised and the control denervated muscles showed a progressive decrease in excitability, this was less marked on the treated side.

At various intervals after recovery sections were removed for biopsy, and in all cases there was a striking difference in the appearance of the exposed muscles. Those on the treated side were larger and more normal to the naked eye. Sections showed the treated muscles to have larger fibres, more definite striation, and less fibrosis than those on the untreated side. Muscles situated superficially showed the more pronounced benefit from the treatment.

The results of these experiments leave no doubt in the minds of the authors that electrotherapy in the treatment of peripheral nerve lesions has a sound scientific basis.

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142

THE CLINICAL APPLICATION OF ELECTROMYOGRAPHY

by G. Weddell, B. Feinstein & R. E. Pattle, *Lancet*, **1**, 236, 20/2/43

When a wasted muscle is examined, a search is made for fibrillation and fasciculation, but only marked fibrillation can be seen, and even this is visible only in the superficial muscles in thin subjects. More exact information may be obtained by observations of the electrical activity of muscles. Recent progress in the study of the electrical behaviour of muscles in health and disease shows that many of the conclusions upon the presence or absence of fibrillation which have been based upon direct observation should be revised.

The present authors, working at a Military Hospital for Head Injuries and in the Departments of Anatomy and Orthopædic Surgery at Oxford, have done much to simplify the use of electromyography in clinical diagnosis, and they have confirmed many of the observations made previously on this subject by Denny-Brown & Pennybacker (1938). Their conclusions may be summarised as follows:

(i) When, more than three weeks after an injury, there is a sustained slight motor activity on attempted movement (even when the movement is not visible), and an absence of fibrillation potentials, it may be concluded that no axons have been cut and there is only a transient nerve block.

(ii) A mixture of fibrillation and motor unit action potentials means either a partial interruption or incomplete regeneration of the nerve. When there is doubt about the presence of fibrillation, a novocaine nerve block will stop the motor unit activity and so simplify the record.

(iii) When there are fibrillation action potentials without motor unit activity, there is complete section of the lower motor neurone. When denervated muscle does not respond to ordinary galvanic stimuli, electromyography is particularly helpful in determining the true condition of the nerve.

(iv) A mixture of fibrillation action potentials and a peculiar form of discharge called by the authors "nascent" motor unit potentials, shows that innervation is returning to the muscle.

(v) When action potentials resembling those of fibrillation follow insertion of a needle electrode into a muscle which shows no motor unit activity, there is complete interruption of the nerve. This provoked fibrillation activity is found either before true fibrillation appears or after it has ceased, and also immediately before "nascent" action potentials appear. This increased irritability therefore adds information in the absence of fibrillation.

(vi) When there is no electrical activity at all in a muscle, more than a few weeks after an injury, complete replacement of the muscle by fibrous tissue has occurred.

These conclusions show how much extra information can be obtained by means of electromyography in most cases of peripheral nerve damage. The method which the authors used is a simple one—the insertion into the muscle of a concentric needle electrode made from a small hypodermic needle, and connected to a high-gain amplifier which activates a cathode ray oscillograph and a loud speaker. The low-pitched noise of the motor unit potential is easily differentiated from the sharp clicking of fibrillation, and the oscillograph records, of which an example is given, can also be interpreted with ease.

In a denervated muscle the amount of fibrillation varies directly with the temperature, and it can be found in every case of muscle wasting if the muscle is warmed. Experiments on animals show that the time of onset of fibrillation varies with the size of the animal—mouse 3½ days, rat 4, rabbit 6, monkey 8 and man 18 in comparable muscles. As the time is lengthened by thyroidectomy, it seems that this variation is due to the different metabolic rates of the animals. The authors, on the other hand, found no direct correlation between the degree of fibrillation and the speed of wasting, so that the theory that wasting is due to the over-activity which results from fibrillation in wasted muscle appears to be false.

The electromyogram is used clinically by inserting the needle electrode into two or three places in the belly of the muscle and observing the electrical activity directly. Thus an exact record can be obtained of the state of all the muscles in the affected region and their progress can be followed by re-examination from time to time. Also the state of different parts of the same muscle can be compared, and the authors describe a case where the method led to the correct diagnosis when only the distal half of a muscle was denervated. As such a delicate method of examination is available, the level of a spinal cord lesion can be checked by observing which muscles are showing evidence of lower motor neurone denervation—for instance the presence of fibrillation, diminished motor unit activity, or of "nascent" potentials in an intercostal muscle will give an exact localisation of the position of a thoracic cord lesion.

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Printed by Spottiswoode, Ballantyne and Co. Ltd., Colchester, London and Eton